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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,569	09/21/2000	R. Rogers Yocum	BGI-141CP	8755

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LAHIVE & COCKFIELD
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BOSTON, MA 02109

EXAMINER

STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/667,569

Applicant(s)

YOCUM ET AL.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) See Continuation Sheet are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 1,2,7,12,14-44,46-53,62,67-75,82,83,88,90,97,99,102,104,106 and 108-110.

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 1,2,7,12,14-44,46-53,62,67-75,82,83,88,90,97,99,102,104,106 and 108-110.

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DETAILED ACTION***Application Status***

The instant Office action is a supplemental restriction requirement. The previous Office action (Paper No. 7) was a restriction requirement of pending Claims 1, 2, 7, 12, 14-44, 46-53, 62, 67-75, 82, 83, 88, 90, 97, 99, 102, 104, 106, and 108-110. Applicants' election without traverse of Group I, claims 1, 2, 7, 12, 14-34, 36, 37, 39-44, 46-50, and 51, amendment to claim 41, and cancellation of claim 98 in Paper No. 10 is acknowledged.

It is noted that applicants state in Paper No. 10 that claims 35, 38, 52, 53, 62, 67-75, 82, 83, 88, 90, 97, 99, 102, 104, 106, and 108-110 have been cancelled. However, the examiner can find no amendment directing cancellation of said claims.

This supplemental requirement is at the discretion of the Examiner (see MPEP 802 and 37 CFR 1.142) and is deemed appropriate and necessary in view of the plurality of patentably distinct inventions in each of Groups I-V of the restriction of Paper No. 7.

Claims 1, 2, 7, 12, 14-44, 46-53, 62, 67-75, 82, 83, 88, 90, 97, 99, 102, 104, 106, and 108-110 are pending in the application.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claim(s) 1, 2, 7, 12, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated isoleucine-valine (*ilv*) pathway, overexpressing acetohydroxyacid synthetase encoded by an *ilvBN* nucleic acid sequence, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129.

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- II. Claim(s) 1, 2, 7, 12, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector comprising an *alsS* nucleic acid sequence encoding acetolactate synthase, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129.
- III. Claim(s) 1, 2, 7, 12, 14-19, 21, 24-28, 30, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway and overexpressing acetohydroxyacid isomeroreductase encoded by an *ivC* nucleic acid sequence, and overexpresses ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129.
- IV. Claim(s) 1, 2, 7, 12, 14-19, 22, 24-28, 31, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, overexpressing dihydroxyacid dehydratase encoded by an *ilvD* nucleic acid sequence, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129.
- V. Claim(s) 1, 2, 7, 12, 14-19, 23, 24-28, 32-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus*

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subtilis pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed or independent of aspartate or beta-alanine feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector comprising a *panD* nucleic acid sequence encoding aspartate-alpha-decarboxylase, and overexpressing ketopantoate reductase encoded by a *panE1* nucleic acid sequence, classified in class 435, subclass 129.

- VI. Claim(s) 1, 2, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated isoleucine-valine (*ilv*) pathway, overexpressing acetohydroxyacid synthetase encoded by an *ilvBN* nucleic acid sequence, and overexpressing ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129.
- VII. Claim(s) 1, 2, 14-20, 24-29, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector comprising an *alsS* nucleic acid sequence encoding acetolactate synthase, and overexpressing ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129.

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- VIII. Claim(s) 1, 2, 14-19, 21, 24-28, 30, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway and overexpressing acetohydroxyacid isomeroreductase encoded by an *ivC* nucleic acid sequence, and overexpresses ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129.
- IX. Claim(s) 1, 2, 14-19, 22, 24-28, 31, 33-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* s pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway and overexpressing dihydroxyacid dehydratase encoded by an *ilvD* nucleic acid sequence, and overexpresses ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129.
- X. Claim(s) 1, 2, 14-19, 23, 24-28, 32-35, drawn to a method of producing a panto-compound comprising culturing a microorganism that overexpresses a *Bacillus* or *Bacillus subtilis* pantothenate biosynthetic enzyme, a method of producing pantothenate in a manner independent of precursor feed or independent of aspartate or beta-alanine feed by culturing a microorganism overexpressing aspartate-alpha-decarboxylase having a deregulated *ilv* pathway, transformed with a vector comprising a *panD* nucleic acid sequence encoding aspartate-alpha-decarboxylase, and overexpresses ketopantoate hydroxymethyltransferase (*panB*) and pantothenate synthetase (*panC*) or transformed with a *panBCD* nucleic acid sequence, classified in class 435, subclass 129.

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- XI. Claim(s) 36-38, drawn to a method of producing beta-alanine by culturing a microorganism overexpressing aspartate-alpha-decarboxylase and having a mutation in a nucleic acid encoding ketopantoate hydroxymethyltransferase, classified in class 435, subclass 116.
- XII. Claim(s) 39-44, 46, 47, 50, 51, drawn to a method for enhancing production of a panto-compound by culturing a microorganism having a mutant pantothenate kinase encoded by a mutant *coaX* and *coaA* genes, classified in class 435, subclass 129.
- XIII. Claim(s) 41, 46, 47, 48, 50, 51, drawn to a method for enhancing production of a panto-compound by culturing a microorganism having a mutant pantothenate kinase and having a deregulated *ilv* biosynthetic pathway, classified in class 435, subclass 129.
- XIV. Claim(s) 41, 42, 46, 47, 49, 50, 51, drawn to a method for enhancing production of a panto-compound by culturing a microorganism having a mutant pantothenate kinase and overexpressing *panD* encoding aspartate-alpha-decarboxylase and *panE* encoding ketopantoate reductase, classified in class 435, subclass 129.
- XV. Claim(s) 52, 53, drawn to a method for identifying compounds that modulate pantothenate kinase activity by contacting a cell expressing pantothenate kinase encoded by a *coaX* gene and a *coaA* gene, classified in class 435, subclass 15.
- XVI. Claim(s) 62, 67-69, 71-75, 83, 88, 99, 108, drawn to a recombinant microorganism overexpressing a *Bacillus* pantothenate biosynthetic enzyme, a nucleic acid molecule comprising a mutant *coaX* gene, a vector comprising a mutant *coaX* nucleic acid, a recombinant microorganism having mutant *coaX* and *coaA* genes, classified in class 435, subclass 252.31.
- XVII. Claim(s) 70, 83, 90, 99, 109, drawn to a nucleic acid comprising a *coaX* gene, a vector comprising a *coaX* said nucleic acid, classified in class 536, subclass 23.2.
- XVIII. Claim(s) 82, drawn to a recombinant microorganism, classified in class 435, subclass 252.31.

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- XIX. Claim(s) 83, 97, drawn to a vector, classified in class 435, subclass 320.1.
- XX. Claim(s) 102, 104, drawn to a *Bacillus* ketopantoate reductase polypeptide, classified in class 435, subclass 190.
- XXI. Claim(s) 102, 106, drawn to a *Bacillus* aspartate-alpha-decarboxylase polypeptide, classified in class 435, subclass 232.
- XXII. Claim(s) 102, 110, drawn to an isolated pantothenate kinase protein encoded by a *coaX* gene, classified in class 435, subclass 194.
2. For each of inventions I-X above, restriction to one of the following mutant genes is also required under 35 USC 121. Therefore, election is required of one of inventions I-X and one of inventions (A)-(D).
- (A). a mutant *avtA* gene encoding valine-pyruvate amino acid transferase.
- (B). a mutant *ilvE* gene encoding a branched-chain amino acid transferase.
- (C). a mutant *ansB* gene encoding an asparaginase.
- (D). a mutant *alsD* gene encoding acetolactate decarboxylase.
3. If applicant should elect the invention of Group XVII, restriction to one of the following recombinant microorganisms is also required under 35 USC 121. Therefore, if applicant elects Group XVIII, an election is also required to of one of inventions (E)-(AB).

(E)	PA221	(M)	PA412	(U)	PA404
(F)	PA235	(N)	PA413	(V)	PA405
(G)	PA236	(O)	PA303	(W)	PA374
(H)	PA313	(P)	PA327	(X)	PA354
(I)	PA410	(Q)	PA328	(Y)	PA365
(J)	PA402	(R)	PA401	(Z)	PA377
(K)	PA403	(S)	PA340	(AA)	PA651
(L)	PA411	(T)	PA342	(AB)	PA824

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4. If applicant should elect the invention of Group XIX, restriction to one of the following recombinant vectors is also required under 35 USC 121. Therefore, if applicant elects Group XIX, an election is also required to of one of inventions (AC)-(AW).

(AC)	pAN004	(AJ)	pAN441	(AQ)	pAN263
(AD)	pAN005	(AK)	pAN442	(AR)	pAN240
(AE)	pAN006	(AL)	pAN443	(AS)	pAN294
(AF)	pAN236	(AM)	pAN251	(AT)	pAN296
(AG)	pAN423	(AN)	pAN267	(AU)	pAN336
(AH)	pAN428	(AO)	pAN256	(AV)	pAN341
(AI)	pAN429	(AP)	pAN257	(AW)	pAN342

5. The inventions are distinct, each from the other because:

The nucleic acids and the nucleic acids used to transform the microorganisms of Groups XVI-XIX and (A)-(AW) are distinct because each of the nucleic acids represents a structurally distinct nucleic acid sequence. Therefore, where structural identity is required, such as for hybridization or polypeptide expression, the different nucleic acid sequences have different effects. Furthermore, each of the nucleic acids is patentably distinct as one of the nucleic acids would not render the others obvious.

6. The polypeptides of Groups XX-XXII are distinct because each of the polypeptides represents a structurally distinct amino acid sequence. Therefore, where structural identity is required, such as for the production of antibodies, the different sequences have different effects. Furthermore, each of the polypeptides is patentably distinct as one of the polypeptides would not render the others obvious.

7. The nucleic acids and nucleic acids used to transform the microorganisms of Groups XVI-XIX and (A)-(AW) and the polypeptides of Groups XX-XXII each comprises a chemically unrelated structure capable of separate manufacture, use and effect. The nucleic acids of Groups XVI-XIX and (A)-(AW) have other utility besides encoding polypeptides such as a hybridization probe and the polypeptides of Groups XX-XXII can be made by a method independent of said nucleic acids such as purification from the natural source or *in vitro* synthesis.

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8. The polypeptides of Groups XX-XXII are unrelated to the method(s) of Groups I-XV as they are neither used nor made by the method(s) of Groups I-XV.

9. The nucleic acids and microorganisms of Groups XVI-XIX and (A)-(AW) and the methods of Groups I-XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids and microorganisms of Groups XVI-XIX and (A)-(AW) can be used for expression of the polypeptides of Groups XX-XXII.

10. The methods of Group I-XV are independent as they comprise different steps, utilize different products and/or yield different results.

11. It is noted that claims 20, 25, 26, 27, 29, 33, 34, 35, 37, 49, 50, 82, and 97 will be examined to the extent the claims read on the elected subject matter.

12. The inventions listed as Groups I-XXII and (A)-(AW) require divergent patent and non-patent literature and sequence searches, thus establishing the serious burden of search on the examiner.

13. Because these inventions are distinct for the reasons given above and each of the inventions listed as Groups I-XXII and (A)-(AW) requires a separate search, restriction for examination purposes as indicated is proper. "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 808.02" (see MPEP 803).

Conclusion

14. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

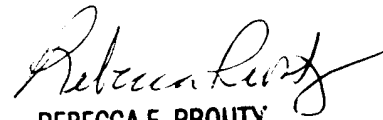
15. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of

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inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~
1605